

Titre: Anionic surfaces with minimal charge density can restore burst coagulation of microparticle/exosome-depleted blood plasma

Title: Contreras-Garcia Angel, Maxime Desgagné, Noelia D'Elia,

Auteurs: Lafantaisie-Favreau Charles-Hubert, Ruiz Juan Carlos, Rivard

Authors: Georges-Etienne, Michael R. Wertheimer, Messina Paula, & Hoemann Caroline

Date: 2016

Type: Communication de conférence / Conference or Workshop Item

Angel, C.-G., Desgagné, M., D'Elia, N., Charles-Hubert, L.-F., Juan Carlos, R.,

Georges-Etienne, R., Wertheimer, M. R., Paula, M., & Caroline, H. (2016, May).

Référence: Anionic surfaces with minimal charge density can restore burst coagulation of microparticle/exosome-depleted blood plasma [Poster]. 10th World Biomaterials Congress, Montréal, Québec (2 pages). Published in *Frontiers in Bioengineering and Biotechnology*, 4. <https://doi.org/10.3389/conf.fbioe.2016.01.02632>

Document en libre accès dans PolyPublie

Open Access document in PolyPublie

URL de PolyPublie: <https://publications.polymtl.ca/4751/>

PolyPublie URL:

Version: Version officielle de l'éditeur / Published version
Non révisé par les pairs / Unrefereed

Conditions d'utilisation: CC BY
Terms of Use:

Document publié chez l'éditeur officiel

Document issued by the official publisher

Nom de la conférence: 10th World Biomaterials Congress
Conference Name:

Date et lieu: 2016-05-17 - 2016-05-22, Montréal, Québec
Date and Location:

Maison d'édition: Frontiers
Publisher:

URL officiel: <https://doi.org/10.3389/conf.fbioe.2016.01.02632>
Official URL:

Mention légale:
Legal notice:

EVENT ABSTRACT

[« Back to Event](#)

Anionic surfaces with minimal charge density can restore burst coagulation of microparticle/exosome-depleted blood plasma

Angel Contreras-Garcia¹, Desgagné Maxime², D'Elia L. Noelia³, Charles-Hubert Lafantaisie-Favreau⁴, Juan Carlos Ruiz⁵, Georges-Etienne Rivard⁶, Wertheimer Michel¹, Paula Messina³ and Caroline D. Hoemann^{2,4}

¹ Ecole Polytechnique, Engineering Physics, Canada

² Ecole Polytechnique, Chemical Engineering, Canada

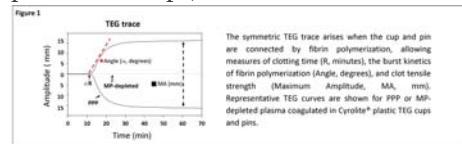
³ Universidad Nacional del Sur, Chemistry, Argentina

⁴ Ecole Polytechnique, Institute of Biomedical Engineering, Canada

⁵ Universidad Autónoma Metropolitana-Iztapalapa, Basic Sciences and Engineering, Chemical Engineering, Mexico

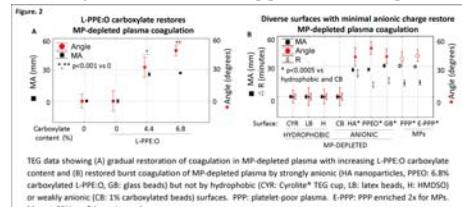
⁶ Hôpital Sainte Justine, Division of Hematology-Oncology, Canada

Introduction: Blood contains microparticles (MP) and exosomes derived from a variety of cell types including activated platelets. MPs are procoagulant because their surfaces can express tissue factor and/or calcium-binding sites for coagulation factors that cooperate to induce burst thrombin activation [1]. Platelet-poor plasma (PPP) contains low levels of MPs and can be induced to coagulate after contact with both hydrophilic and hydrophobic surfaces [2]. In a standard thromboelastography (TEG) assay with plastic cups and pins, PPP undergoes spontaneous burst coagulation, as revealed in the TEG trace by a variable clotting time (10 to 26 minutes), a low Angle ($\sim 33^\circ$) and reproducible low clot tensile strength or Maximum Amplitude (MA ~ 28 mm) [3] (Fig. 1). PPP coagulates faster and more reproducibly in TEG cups and pins coated with anionic carboxylate-rich nanolayers suggesting FXII activation [2], however the role of MPs is unclear. This study tested the hypothesis that MPs are necessary for PPP burst coagulation in plastic TEG cups, and that anionic surfaces are sufficient to restore burst coagulation of MP-depleted plasma.



Materials and Methods: Plastic Cyrolite® TEG cups and pins (Hemoscope, IN, USA) were modified by plasma-enhanced chemical vapor deposition to make hydrophobic (PP-HMDSO, poly(hexamethyldisiloxane) or variable anionic (L-PPE:O, 0, 4.4% or 6.8% carboxylate functional group content) nanocoatings [3]. Coagulation in the TEG cup was initiated by combining i) human citrated PPP (Precision Biologics, NS, Canada), ii) MP-depleted plasma (by ultracentrifugation 150,000xg, 30 min) or iii) PPP 2xenriched for MP, with 20 μ L of 200 mM CaCl₂ containing 2.5 mg/mL 10 μ m diameter beads (latex, borosilicate glass, carboxylated plastic), or 0.25 to 25 mg/mL hydroxyapatite (HA) nanoparticles (2.03 Ca/P ratio) [4]. Bead composition was analyzed by XPS. Statistical tests used ANOVA (Statistica).

Results: Glass beads with 9% Si and 4% Ca content triggered the fastest PPP clotting time ($p < 0.05$ vs all hydrophobic surfaces). PPP burst coagulation was enhanced by glass beads, L-PPE:O (6.8% carboxylate), and HA nanoparticles, as shown by the Angle increasing from 36° to $>55^\circ$. HA nanoparticles accelerated PPP burst coagulation in a dose-dependent manner ($p = 0.004$). MP-depleted plasma failed to clot in plastic TEG cups (Fig. 1), and burst coagulation was progressively restored by L-PPE:O with 4.4 to 6.8% carboxylate content ($p < 0.001$, Fig. 2A). MP-depleted plasma coagulation was also induced by 2.5 mg/mL glass beads and 25 mg/mL HA nanoparticles but not by Latex beads, HMDSO, or 1% carboxylated beads (Fig. 2B). In MP-depleted plasma, L-PPE:O with 6.8% carboxylate content triggered the highest Angle (50°) with a clot tensile strength similar to PPP and MP-enriched PPP (Fig. 2B).



Discussion: Glass beads, >4.4% carboxylated surfaces and HA were effective MP biomimetics that restored burst coagulation. These results suggest that inorganic anionic surfaces can serve as functional binding sites for the calcium-binding gla domain of factors

FIXa, FXa and prothrombin. This study is consistent with the notion that tenase and prothrombinase form side-by-side on the same anionic surface [1].

Conclusions: A minimal 6.8% anionic charge group density is required to bring tenase and prothrombinase in close physical proximity for optimal cooperative behavior.

Funding: Natural Sciences and Engineering Research Council of Canada (NSERC) and the Canadian Institutes of Health Research (CIHR). Salary support was from the Fonds de la Recherche Québec Snaté (FRQ-S), CONACyT (México), MEDITIS Program (NSERC and Ecole Polytechnique), Emerging Leaders in the Americas Program, and The Arthritis Society (Canada)

References:

- [1] Owens, A.P., III and N. Mackman, Microparticles in Hemostasis and Thrombosis. *Circulation Research*, 2011;108(10): 1284-1297.
- [2] Zhuo, R., C.A. Siedlecki, and E.A. Vogler, Autoactivation of Blood Factor XII at Hydrophilic and Hydrophobic Surfaces. *Biomaterials*, 2006;27(24):4325-4332.
- [3] Contreras-García, A., Y. Merhi, J.-C. Ruiz, M.R. Wertheimer, C.D. Hoemann, Thromboelastography (TEG) cups and Pins with Different PECVD Coatings: Effect on the Coagulation Cascade in Platelet-poor Blood Plasma. *Plasma Processes and Polymers*, 2013;10(9):817-828.
- [4] D'Elia, N.L., N. Gravina, J.M. Russo, J.A. Laiuppa, G.E. Santillan, P.V. Messina, Manipulating the bioactivity of hydroxyapatite nano-rods structured networks: Effects on mineral coating morphology and growth kinetic. *Biochimica Biophysica Acta-General Subjects*, 2013; 1830(11):5014-5026.

Keywords: Biomimetic, Bioactivity, surface property, Polymeric material **Conference:** 10th World Biomaterials Congress, Montréal, Canada, 17 May - 22 May, 2016.

Presentation Type: Poster **Topic:** Protein interactions with biomaterials

Citation: Contreras-García A, Maxime D, Noelia DL, Lafontaisie-Favreau C, Ruiz J, Rivard G, Michel W, Messina P and Hoemann CD (2016). Anionic surfaces with minimal charge density can restore burst coagulation of microparticle/exosome-depleted blood plasma. *Front. Bioeng. Biotechnol. Conference Abstract: 10th World Biomaterials Congress*. doi: 10.3389/conf.FBIOE.2016.01.02632

Copyright: The abstracts in this collection have not been subject to any Frontiers peer review or checks, and are not endorsed by Frontiers. They are made available through the Frontiers publishing platform as a service to conference organizers and presenters.

The copyright in the individual abstracts is owned by the author of each abstract or his/her employer unless otherwise stated.

Each abstract, as well as the collection of abstracts, are published under a Creative Commons CC-BY 4.0 (attribution) licence (<https://creativecommons.org/licenses/by/4.0/>) and may thus be reproduced, translated, adapted and be the subject of derivative works provided the authors and Frontiers are attributed.

For Frontiers' terms and conditions please see <https://www.frontiersin.org/legal/terms-and-conditions>. Received: 27 Mar 2016; Published Online: 30 Mar 2016.